

**AMENDMENT**

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

**IN THE CLAIMS:**

Kindly amend the claims, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, to read as follows:

1. (Withdrawn) A method of manufacturing a composition wherein the composition comprises an agent which lowers levels of 11 $\beta$ -HSD1.
2. (Withdrawn) The method of claim 1, wherein the composition is used for the promotion of an atheroprotective lipid profile.
3. (Withdrawn) The method of claim 2, wherein 11 $\beta$ -HSD1 levels are lowered by an agent which modulates the expression of the endogenous 11 $\beta$ -HSD1 gene.
4. (Withdrawn) The method of claim 2, wherein 11 $\beta$ -HSD1 levels are lowered by an agent which modulates 11 $\beta$ -HSD1 mRNA transcription or translation.
5. (Withdrawn) The method of claim 4, wherein 11 $\beta$ -HSD1 levels are lowered by an agent which inhibits 11 $\beta$ -HSD1 synthesis or activity.
6. (Withdrawn) The method of claim 5, wherein said agent is selected from the group consisting of carbenoxolone, 11-oxoprogesterone, 3 $\alpha$ ,17,21-trihydroxy-5 $\beta$ -pregnan-3-one, 21-hydroxy-pregn-4-ene-3,11,20-trione, androst-4-ene-3,11,20-trione and 3 $\beta$ -hydroxyandrost-5-en-17-one.
7. (Withdrawn) The method of claim 2, wherein the atheroprotective lipid profile comprises a reduction in plasma triglyceride levels.
8. (Withdrawn) The method of claim 2, wherein the atheroprotective lipid profile comprises an increase in HDL cholesterol levels.
9. (Withdrawn) The method of claim 2, wherein serum apoCIII levels are reduced as a consequence of the reduction of 11 $\beta$ -HSD1 levels.

10. (Withdrawn) The method of claim 2, wherein PPAR $\alpha$  levels are increased as a consequence of the reduction of 11 $\beta$ -HSD1 levels.

11. (Withdrawn) The method of claim 1, wherein the composition is used for increasing insulin sensitivity.

12. (Withdrawn) The method of claim 1, wherein the composition is used for the promotion of glucose tolerance.

13. (Withdrawn) A method of manufacturing a composition for the promotion of an atheroprotective lipid profile which increases insulin sensitivity or promotes glucose tolerance wherein the composition comprises an agent which reduces intracellular 11 $\beta$ -HSD1 activity and a PPAR $\alpha$  agonist.

14. (Currently Amended) A method for reducing cardiovascular disease risk in an animal at risk of cardiovascular disease, comprising administering to said animal a pharmaceutically effective amount of an agent which directly inhibits 11 $\beta$ -HSD1 protein synthesis or 11 $\beta$ -HSD1 reductase activity.

15-17. (Cancelled)

18. (Currently Amended) A method according to claim 14, wherein said agent is selected from the group consisting of ~~the steroids set forth in Table IV of Monder C, and White PC, Vitamins and Hormones 1993; 47: 187-271~~ 11-oxoprogesterone, 3 $\alpha$ ,17,21-trihydroxy-5 $\beta$ -pregnan-3-20-dione, 21-hydroxy-pregn-4-ene-3,11,20-trione, androst-4-ene-3,11,20-trione and 3 $\beta$ -hydroxyandrost-5-en-17-one.

19. (Previously Presented) The method of claim 14, wherein a reduction in plasma triglyceride levels is obtained.

20. (Currently Amended) The method according to claim 14, wherein a reduction in LDL cholesterol levels is obtained.

21. (Previously Presented) The method of claim 14, wherein an increase in HDL cholesterol levels is obtained.

22. (Currently Amended) The method of claim 14, wherein serum apoCIII levels are reduced as a consequence of the inhibition of 11 $\beta$ -HSD1 protein synthesis or 11 $\beta$ -HSD1 reductase activity.

23. (Currently Amended) The method of claim 14 wherein PPAR $\alpha$  and/or PPAR $\gamma$  levels are increased as a consequence of the inhibition of 11 $\beta$ -HSD1 protein synthesis or 11 $\beta$ -HSD1 reductase activity.

24. (Original) The method of claim 14, wherein the agent increases insulin sensitivity risk in an animal at risk of cardiovascular disease.

25. (Original) The method of claim 14, wherein the agent improves glucose tolerance in a animal at risk of cardiovascular disease.

26. (Currently Amended) A method for the promotion of an atheroprotective lipid profile, increasing insulin sensitivity or promoting glucose tolerance, comprising administering to an animal in need thereof an agent which reduces 11 $\beta$ -HSD1 reductase activity and a PPAR $\alpha$  agonist.

27. (Withdrawn) A pharmaceutical composition comprising an agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\alpha$  agonist.

28. (Withdrawn) An agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\alpha$  agonist for simultaneous, simultaneous separate or sequential use in the promotion of an atheroprotective lipid profile, increasing insulin sensitivity or promoting glucose tolerance.

29. (Withdrawn) A kit comprising an agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\alpha$  agonist, for use in the promotion of an atheroprotective lipid profile, increasing insulin sensitivity or promoting glucose tolerance.

30. (Withdrawn) The kit of claim 29, wherein the kit additionally comprises instructions for use.

31. (Withdrawn) The kit of claim 29, wherein the agents are packaged in unit doses.

32. (Withdrawn) A method for the control of cardiovascular risk, increasing insulin sensitivity or promoting glucose tolerance, comprising administering to an animal in need thereof an agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\gamma$  agonist.

32. (Withdrawn) A pharmaceutical composition comprising an agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\gamma$  agonist.

34. (Withdrawn) An agent which reduces 11 $\beta$ -HSD1 activity and a PPAR $\gamma$  agonist for simultaneous, simultaneous separate or sequential use in the control of cardiovascular risk, increasing insulin sensitivity or promoting glucose tolerance.

35. (Withdrawn) A kit comprising an agent which reduces  $11\beta$ -HSD1 activity and a PPAR $\gamma$  agonist, for use in the control of cardiovascular risk, increasing insulin sensitivity or promoting glucose tolerance.
36. (Withdrawn) The kit of claim 35, wherein the kit additionally comprises instructions.
37. (Withdrawn) The kit of claim 35, wherein the agents are packaged in unit doses.
38. (Withdrawn) A method of using an agent which lowers levels of  $11\beta$ -HSD1 in the manufacture of a composition for increasing metabolic rate.
39. (Withdrawn) The method of claim 38, for preventing or reversing an undesired increase in body weight.
40. (Withdrawn) The method of claim 38, wherein the agent which lowers levels of  $11\beta$ -HSD1 is administered in combination with an appetite suppressant.
41. (Withdrawn) The method of claim 38, wherein the agent which lowers levels of  $11\beta$ -HSD1 is administered in combination with an antiobesity drug.
42. (Withdrawn) An inhibitor of  $11\beta$ -HSD1 and a glucocorticoid for simultaneous, simultaneous separate or sequential administration in the treatment of inflammation.
43. (Withdrawn) A method of using an inhibitor of  $11\beta$ -HSD1 in the manufacture of a composition for the prevention of the side-effects of glucocorticoid therapy.
44. (Withdrawn) The method of claim 43, wherein the side-effects are associated with cardiovascular risk, altered lipid profile, insulin resistance, hyperglycaemia, obesity and/or hypertension.
45. (Withdrawn) A method of using an inhibitor of  $11\beta$ -HSD1 in the manufacture of a composition for reducing cholesterol storage in macrophages.
46. (Withdrawn) An inhibitor of  $11\beta$ -HSD1 and an PPAR $\gamma$  agonist for simultaneous, simultaneous separate or sequential use for the reduction of cholesterol storage in macrophages.
47. (Withdrawn) A method of using an inhibitor of  $11\beta$ -HSD1 in the manufacture of a composition for reducing intrahepatic fat levels.
48. (Withdrawn) The method of claim 47, wherein the lipid profile is improved.

49. (Withdrawn) The method of claim 47, wherein hepatic dysfunction is prevented or reversed in patients with non-alcoholic steatohepatitis, including reducing serum transaminases.

50. (Withdrawn) The method of claim 47, wherein progression of non-alcoholic steatohepatitis to cirrhosis is prevented.

51. (Withdrawn) An inhibitor of 11 $\beta$ -HSD1 and metformin for simultaneous, simultaneous separate or sequential use for the reduction of intrahepatic fat levels.

52. (Currently Amended) A method according to claim 14, wherein the agent inhibits ~~at least one biological reductase~~ activity of the 11 $\beta$ -HSD1 protein once produced.

53. (Currently Amended) A method according to claim 14, wherein the agent ~~prevents or~~ downregulates production of the 11 $\beta$ -HSD1 protein from 11 $\beta$ -HSD1 mRNA.